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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/763,362	04/23/2001	Kazuma Tomizuka	081356/0158	4670

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EXAMINER	
TON, THAIAN N	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 05/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/763,362	TOMIZUKA ET AL.	
	Examiner	Art Unit	
	Thaian N. Ton	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-83,85,93,96-112,117-124,126,135,136 and 138* is/are pending in the application.

4a) Of the above claim(s) *26-83 and 85* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *93,96-112,117-124,126,135,136 and 138* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/11/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' Amendment and Response, filed 3/3/06, has been considered. Claims 93 and 117 are amended; claims 26-83, 85, 93, 96-112, 117-124, 126, 135, 136 and 138 are pending; claims 26-83 and 85 are withdrawn from further consideration as being directed to non-elected groups, Applicant timely traversed the restriction (election) requirement in Paper No. 8; claims 93, 96-112, 117-124, 126, 135, 136 and 138 are under current examination.

The Tomizuka Declaration, filed 3/3/06, has been considered, but not found to be fully persuasive.

Information Disclosure Statement

Applicants' IDS, filed 6/11/03, has been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 93, 96-112, 117-124, 126, 135, 136 and 138 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is maintained for reasons of record advanced in the prior Office actions.

The instant invention consists of a recombinant chromosome, comprising the human chromosome #14 centromere of SC20, two telomere sequences, at least one recognition sequence for a site-directed recombination enzyme, at least two

fragments from different human chromosomes, wherein each fragment comprises an antibody gene locus; and a marker gene, wherein the recognition sequence for the site-directed recombination enzyme is located between the chromosome fragments.

Applicants' Arguments. Applicants' argue that the claimed invention is described because, "The determinative issue is not whether the specification makes it possible to later obtain an identical copy of any specific clone. Rather, it is whether the specification provides a repeatable and controlled method for obtaining a chromosome fragment that contains an antibody locus." See page 16, 1st paragraph. Applicants argue that the specification enables one to join chromosome fragments, at least two of which contain antibody loci, to make the claimed recombinant chromosome, and that these fragments can be produced spontaneously or non-spontaneously. Applicants argue that the derivation of particular clones is only tangentially relevant to the fact that the specification provides a reproducible method of obtaining a chromosome fragment that contains an antibody locus. Applicants present the Tomizuka Declaration as evidence to show that the claimed chromosome can be made by both spontaneous and non-spontaneous methods, that the method is reproducible, and that the genetic material that is used in the method is not "essential starting material." See page 16 of the Response. Applicants argue that irradiation is not required to produce the chromosome fragments (p. 18 of the Response).

Tomizuka Declaration. The Declaration states that human antibody genes can be expressed in a non-human organism (such as a mouse), by isolation of intact human chromosomes that contain clusters of antibody genes, such as chromosomes 2, 14, and 22, from a human cell, then truncating the chromosomes with or without the use of irradiation and isolating fragments that contain antibody clusters, and then ligating the resultant fragments with other chromosome fragments to produce the recombinant chromosome (see #10, p. 2 of the Declaration). The Declaration

provides further guidance with regard to various clones that are recited in the specification, for example, that clone 6-1 is essentially identical to A9/#22, but that 6-1 is resistant to both puromycin and G418 neomycin, whereas A9/#22 is only resistant to G418 (#14, p. 3 of the Declaration). The Declaration teaches that the A9/#22 neomycin resistant cells by MMCT without irradiation, by integrating the G418 gene into chromosome #22 of normal human fibroblasts, fusing the cells with mouse A9 cells, via MMCT, and culturing the fused cells on G418 selective media. Cells that contained an unfragmented human chromosome #22 were identified, and then truncated by telomere truncation to produce a desired fragment. (see p. 4, #20).

Response to Arguments and Declaration. Applicants' arguments are found to be partially persuasive. The specification provides guidance with regard to the generation of a fragment that contains an antibody gene locus. However, there is no support or guidance in the specification, nor the Declaration, with regard to the presence of an entire antibody gene locus (as specifically recited in claims 100, 103, for example). For example, Example 82 recites that 2 clones having human lambda gene were identified by polymorphic markers (see page 273). Example 83 recites the targeted truncation of the human chromosome #22, and then PCR detection of various genes and polymorphic markers (p. 276, 1st full paragraph). The same analysis follows in Example 92, which recites that the targeted insertion site is at a CD8A locus, which is closely linked to the Igκ region in the telomere side (p. 305, last ¶). Thus, determination of genes that are closely linked to, or identification of polymorphic markers would at least result in the identification of fragments of various antibody gene loci, however, the specification provides no guidance with regard to the entire gene locus, as instantly encompassed by the claims. An entire gene locus region can encompass upstream, downstream, and non-coding sequences of the locus, for which the specification has neither described, nor provided with guidance to attain. The claims require an entire antibody locus region, however,

the specification fails to provide support as to how to arrive at attaining this. Thus, absent specific teachings with regard to the entire region of the human antibody heavy/light chain locus, and to the extent that the specification fails teach a repeatable method with which to generate these fragments containing the entire region of these loci, the claims are not described. Furthermore, the independent claims, which encompass entire gene loci regions, as well as fragments therefrom, are included in this rejection for the reasons recited above.

Claim Rejections - 35 USC § 112

The prior rejection of claims 93, 96-112, 117-124, 126, 135, 136 and under 35 U.S.C. 112, second paragraph, is withdrawn. The claims now recite that SC20 is contained in the chicken DT-40 cell, and thus, the amendments make the claims definite.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thaian N. Ton whose telephone number is (571) 272-0736. The Examiner can normally be reached on Monday through Thursday from 7:00 to 5:00 (Eastern Standard Time). Should the Examiner be unavailable, inquiries should be directed to Ram Shukla, SPE of Art Unit 1632, at (571) 272-0735. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the Official Fax at (571) 273-8300. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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